

**IN THE CLAIMS:**

Kindly amend the claims as follows:

- 1                   1.   (Previously Amended)   A method of detecting a  
2 malignant tumor in a human subject, comprising:  
3                   (a)   collecting a sample of a bodily substance containing human  
4                   nucleic acid ~~or protein~~, said nucleic acid ~~or protein~~ having  
5                   originated from cells of the human subject;  
6                   (b)   detecting quantitatively or semi-quantitatively in the sample  
7                   a level of expression for ~~laminin  $\alpha$ 4 subunit protein or~~  
8                   laminin  $\alpha$ 4-specific mRNA; and  
9                   (c)   comparing the expression level in (b) to a level of  
10 expression in a normal control, wherein overexpression of  
11 ~~laminin  $\alpha$ 4 subunit protein~~ or laminin  $\alpha$ 4-specific mRNA,  
12 with respect to the control, indicates the presence of a  
13 malignant tumor in the human subject.

- 1                   2.   (Currently Amended)   The method of Claim 1, wherein  
2 the bodily substance is blood, urine, lymph, cerebro-spinal fluid, skin, stroma,  
3 vascular epithelium, oral epithelium, vaginal epithelium, cervical epithelium,  
4 uterine epithelium, intestinal epithelium, bronchial epithelium, esophageal  
5 epithelium, or mesothelium.

- 1                   3.   (Currently Amended)   The method of Claim 1, wherein  
2 the bodily substance is a tissue sample.

1                   4.     (Original)     The method of Claim 3, wherein the tissue  
2     sample is collected from the brain of the subject.

1                   5.     (Original)     The method of Claim 3, wherein the tissue  
2     sample is a tumor tissue.

1                   6.     (Original)     The method of Claim 1, wherein the bodily  
2     substance is plasma.

1                   7.     (Original)     The method of Claim 1, wherein the bodily  
2     substance is a cellular material.

1                   8.     (Original)     The method of Claim 7, wherein the cellular  
2     material is derived from the human subject's brain kidney, bladder, ureter,  
3     urethra, thyroid, parotid gland, submaxillary gland, sublingual gland, lymph  
4     node, bone, cartilage, lung, mediastinum, breast, uterus, ovary, testis,  
5     prostate, cervix uteri, endometrium, pancreas, liver, spleen, adrenal,  
6     esophagus, stomach, or intestine.

1                   9.     (Currently Amended)     The method of Claim 4 7,  
2     wherein the ~~neoplastic growth~~ cellular material is a carcinoma, sarcoma,  
3     lymphoma, mesothelioma, melanoma, glioma, nephroblastoma, glioblastoma,  
4     oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal  
5     tumor, atypical meningioma, malignant meningioma, or neuroblastoma.

1                   10. (Currently Amended)   The method of Claim ~~4~~ 8,  
2   wherein the cellular material is a hyperplastic and/or cytologically dysplastic  
3   cellular growth or proliferation that is benign prostatic hyperplasia/dysplasia or  
4   cervical hyperplasia/dysplasia.

Claims 11 and 12 have been cancelled

1                   13. (Previously Amended)   The method of Claim ~~12~~ 2,  
2   wherein the expression level of laminin  $\alpha$ 4-specific mRNA is detected by  
3   measuring RNA.

1                   14. (Previously Amended)   The method of Claim ~~12~~ 2,  
2   wherein the expression level of laminin 4-specific mRNA is detected by  
3   measuring cDNA.

1                   15. (Previously Amended)   The method of Claim ~~12~~ 2,  
2   wherein a gene expression microarray is used to detect the level of expression  
3   of laminin  $\alpha$ 4-specific mRNA.

1                   16. (Previously Amended)   The method of Claim 1, further  
2   comprising detecting the overexpression of ~~laminin  $\beta$ 1 subunit protein or~~  
3   laminin  $\beta$ 1 subunit protein or *laminin  $\beta$ 1*-specific mRNA relative to the normal  
4   control.

1                   17. (Original Claim) The method of Claim 1, further  
2 comprising detecting quantitatively or semi-quantitatively in the sample a level  
3 of expression with respect to a normal control, of a gene encoding a protein  
4 selected from the group consisting of insulin-like growth factor binding protein  
5 precursor 3, transforming growth factor- $\beta$ -induced gene, vascular endothelial  
6 growth factor, connective tissue growth factor, human insulin-like growth  
7 factor binding protein precursor 5, placental growth factor, transcription factor  
8 Ap-2, human insulin-like growth factor II, epidermal growth factor receptor,  
9 matrix metalloproteinase-2, keratin 18, vimentin, fibronectin 1, phospholipase  
10 A2 receptor, desmoplakin, tropomodulin, tenascin C, and collagen type IV  $\alpha$ 1  
11 chain, or detecting a combination of expression levels for any of these.

1                   18. (Previously Amended) A method of diagnosing the  
2 presence of a glioma in a human subject, comprising:  
3                   (a) obtaining a sample from the brain of the human subject;  
4                   (b) detecting quantitatively or semi-quantitatively in the sample  
5 a level of expression for ~~laminin  $\alpha$ 4 subunit protein or~~  
6 *laminin  $\alpha$ 4-specific mRNA*; and  
7                   (c) comparing the expression level in (b) to a level of  
8 expression in a normal control, wherein overexpression of  
9 ~~laminin  $\alpha$ 4 subunit protein or~~ *laminin  $\alpha$ 4-specific mRNA*,  
10 with respect to the control, indicates the presence of  
11 glioma in the subject.

Claims 19 and 20 have been cancelled.

1                   21. (Previously Amended) The method of Claim 18 ~~20~~,  
2 wherein the expression level of *laminin*  $\alpha$ 4-specific mRNA is detected by  
3 measuring RNA.

1                   22. (Previously Amended) The method of Claim 18 ~~20~~,  
2 wherein the expression level of *laminin*  $\alpha$ 4-specific mRNA is detected by  
3 measuring cDNA.

1                   23. (Previously Amended) The method of Claim 18 ~~20~~,  
2 wherein a gene expression microarray is used to detect the level of expression  
3 of *laminin*  $\alpha$ 4-specific mRNA.

1                   24. (Previously Amended) The method of Claim 18, further  
2 comprising detecting the overexpression of ~~laminin  $\beta$ 1 subunit protein or~~  
3 *laminin*  $\beta$ 1-specific mRNA relative to the normal control.

1                   25. (Original Claim) The method of Claim 18, further  
2 comprising detecting quantitatively or semi-quantitatively in the sample a level  
3 of expression with respect to a normal control, of a gene encoding a protein  
4 selected from the group consisting of insulin-like growth factor binding protein  
5 precursor 3, transforming growth factor- $\beta$ -induced gene, vascular endothelial  
6 growth factor, connective tissue growth factor, human insulin-like growth  
7 factor binding protein precursor 5, placental growth factor, transcription factor  
8 Ap-2, human insulin-like growth factor II, epidermal growth factor receptor,  
9 matrix metalloproteinase-2, keratin 18, vimentin, fibronectin 1, phospholipase  
10 A2 receptor, desmoplakin, tropomodulin, tenascin C, and collagen type IV  $\alpha$ 1  
11 chain, or detecting a combination of expression levels for any of these.

1                   26. (Original Claim)    The method of Claim 18, wherein the  
2   sample is a tumor tissue.

1                   27. (Original Claim)    The method of Claim 18, wherein the  
2   sample comprises plasma.

1                   28. (Previously Amended)   A method of predicting the  
2   recurrence of a malignant tumor in a human subject from whom a tumor has  
3   been resected, comprising:

4                   (a) obtaining a tissue sample from the human subject, said tissue  
5                   sample being from a region adjacent to the site of the  
6                   tumor;

7                   (b) detecting quantitatively or semi-quantitatively a level of  
8                   expression for ~~laminin  $\alpha$ 4 subunit protein or laminin  $\alpha$ 4-~~  
9                   specific mRNA in the sample; and

10                  (c) comparing the expression level in (b) to a level of expression  
11                  in a normal tissue control, wherein overexpression of  
12                  ~~laminin  $\alpha$ 4 subunit protein or laminin  $\alpha$ 4-specific~~ mRNA,  
13                  with respect to the control, is predictive of a recurrence of  
14                  a malignant tumor in the subject.

1                   29. (Original Claim)    The method of Claim 28, wherein the  
2   tissue sample is histopathologically normal in appearance.

Claims 30 and 31 have been cancelled.

1                   32. (Previously Amended) The method of Claim 28 ~~31~~,  
2 wherein the expression level of laminin  $\alpha$ 4-specific mRNA is detected by  
3 measuring RNA.

1                   33. (Previously Amended) The method of Claim 28 ~~31~~,  
2 wherein the expression level of laminin  $\alpha$ 4-specific mRNA is detected by  
3 measuring cDNA.

1                   34. (Previously Amended) The method of Claim 28 ~~31~~,  
2 wherein a gene expression microarray is used to detect the level of expression  
3 of *laminin  $\alpha$ 4*-specific mRNA.

1                   35. (Original Claim) The method of Claim 28, further  
2 comprising detecting quantitatively or semi-quantitatively in the sample a level  
3 of expression with respect to a normal tissue control, of a gene encoding a  
4 protein selected from the group consisting of insulin-like growth factor binding  
5 protein precursor 3, transforming growth factor- $\beta$ -induced gene, vascular  
6 endothelial growth factor, connective tissue growth factor, human insulin-like  
7 growth factor binding protein precursor 5, placental growth factor,  
8 transcription factor Ap-2, human insulin-like growth factor II, epidermal growth  
9 factor receptor, matrix metalloproteinase-2, keratin 18, vimentin, fibronectin  
10 1, phospholipase A2 receptor, desmoplakin, tropomodulin, tenascin C, and  
11 collagen type IV  $\alpha$ 1 chain, or detecting a combination of expression levels for  
12 any of these.

1                   36. (Previously Amended) The method of Claim 28, further  
2 comprising detecting the overexpression of ~~laminin  $\beta$ 1 subunit protein or~~  
3 *laminin  $\beta$ 1-specific mRNA* ~~nucleic acid~~ relative to the normal tissue control.

Claims 37-43 are cancelled.

1                   44. (Previously Amended) A method of predicting the  
2 recurrence of a glioma in a human subject from whom a glioma has been  
3 resected, comprising:  
4                   (a) obtaining a tissue sample from the brain of the human  
5                   subject, said tissue sample being from a region adjacent to  
6                   the site of the glioma;  
7                   (b) detecting quantitatively or semi-quantitatively a level of  
8                   expression for ~~laminin  $\alpha$ 4 subunit protein or~~ *laminin  $\alpha$ 4-*  
9                   specific mRNA in the sample; and  
10                  (c) comparing the expression level in (b) to a level of expression  
11                   in a normal tissue control, wherein overexpression of  
12                   ~~laminin  $\alpha$ 4 subunit protein or~~ *laminin  $\alpha$ 4-specific mRNA*,  
13                   with respect to the control, is predictive of a recurrence of  
14                   glioma in the subject.

1                   45. (Original Claim) The method of Claim 44, wherein the  
2 tissue sample is histopathologically normal in appearance.

Claims 46-47 are cancelled.



1                   48. (Previously Amended) The method of Claim 44 ~~47~~,  
2 wherein the expression level of *laminin*  $\alpha$ 4-specific mRNA is detected by  
3 measuring RNA.

1                   49. (Previously Amended) The method of Claim 44 ~~47~~,  
2 wherein the expression level of *laminin*  $\alpha$ 4-specific mRNA is detected by  
3 measuring cDNA.

1                   50. (Previously Amended) The method of Claim 44 ~~47~~,  
2 wherein a gene expression microarray is used to detect the level of expression  
3 of *laminin*  $\alpha$ 4-specific mRNA.

1                   51. (Original Claim) The method of Claim 44, further  
2 comprising detecting quantitatively or semi-quantitatively in the sample a level  
3 of expression with respect to a normal tissue control, of a gene encoding a  
4 protein selected from the group consisting of insulin-like growth factor binding  
5 protein precursor 3, transforming growth factor- $\beta$ -induced gene, vascular  
6 endothelial growth factor, connective tissue growth factor, human insulin-like  
7 growth factor binding protein precursor 5, placental growth factor,  
8 transcription factor Ap-2, human insulin-like growth factor II, epidermal growth  
9 factor receptor, matrix metalloproteinase-2, keratin 18, vimentin, fibronectin  
10 1, phospholipase A2 receptor, desmoplakin, tropomodulin, tenascin C, and  
11 collagen type IV  $\alpha$ 1 chain, or detecting a combination of expression levels for  
12 any of these.

1                   52. (Previously Amended) The method of Claim 44, further  
2 comprising detecting the overexpression of ~~laminin  $\beta$ 1 subunit protein~~ or  
3 *laminin  $\beta$ 1*-specific mRNA ~~nucleic acid~~ relative to the normal tissue control.

1                   53. (Original Claim) A method of predicting recurrence of a  
2 glioma in a human subject from whom a glioma has been resected,  
3 comprising:  
4                   (a) obtaining a tissue sample from the brain of a human  
5 subject, said tissue sample being from a region adjacent to  
6 the site of the glioma, said sample comprising a cell  
7 expressing a plurality of mRNA species that are detectably  
8 distinct from one another;  
9                   (b) detecting quantitatively or semi-quantitatively an  
10 expression level for *laminin  $\alpha$ 4*-specific mRNA; and  
11                   (c) comparing the expression level in (b) to a level of expression  
12 in a normal tissue control, wherein overexpression of  
13 *laminin  $\alpha$ 4*-specific mRNA, with respect to the control, is  
14 predictive of a recurrence of glioma in the subject.

1                   54. (Original Claim) The method of Claim 53, wherein a  
2 gene expression microarray is used to detect the level of expression of *laminin*  
3  *$\alpha$ 4*-specific mRNA.

1                   55. (Original Claim) The method of Claim 54, wherein the  
2 expression level of *laminin  $\alpha$ 4*-specific mRNA is detected by measuring RNA.

1                   56. (Original Claim)    The method of Claim 54, wherein the  
2   expression level of *laminin*  $\alpha 4$ -specific mRNA is detected by measuring cDNA.

1                   57. (Original Claim)    The method of Claim 53, further  
2   comprising detecting quantitatively or semi-quantitatively in the sample a level  
3   of expression with respect to a normal tissue control, of a growth factor-  
4   related gene encoding a protein selected from the group consisting of insulin-  
5   like growth factor binding protein precursor 3, transforming growth factor- $\beta$ -  
6   induced gene, vascular endothelial growth factor, connective tissue growth  
7   factor, human insulin-like growth factor binding protein precursor 5, placental  
8   growth factor, transcription factor Ap-2, human insulin-like growth factor II,  
9   and epidermal growth factor receptor, whereby the relative aggressiveness of  
10  the glioma is predicted.

1                   58. (Original Claim)    The method of Claim 53, further  
2   comprising detecting quantitatively or semi-quantitatively in the sample a level  
3   of expression with respect to a normal tissue control, of a structural gene  
4   encoding a protein selected from the group consisting of matrix  
5   metalloproteinase-2, keratin 18, vimentin, fibronectin 1, phospholipase A2  
6   receptor, desmoplakin, tropomodulin, tenascin C, and collagen type IV  $\alpha 1$   
7   chain, whereby the relative invasiveness of the glioma is predicted.

1                   59. (Original Claim)    The method of Claim 53, further  
2   comprising detecting the overexpression of *laminin*  $\beta 1$ -specific mRNA relative  
3   to the normal tissue control.

- 1                   60. (Presently Amended) A method of ~~classifying~~  
2 establishing a ~~the~~ grade of a malignant tumor in a human subject, wherein said  
3 grade ranks tumors in terms of invasiveness and aggressiveness, comprising:  
4                   (a) obtaining a tissue sample from the human subject, said  
5 sample comprising a cell expressing a plurality of mRNA  
6 species that are detectably distinct from one another;  
7                   (b) detecting quantitatively or semi-quantitatively an  
8 expression level for at least two of the plurality of mRNA  
9 species, wherein at least one of the detected mRNA  
10 species is a *laminin*  $\alpha$ 4-specific mRNA and at least one is  
11 specific to a growth factor-related gene or to a structural  
12 gene other than a laminin gene;  
13                   (c) constructing an expression profile of the sample comprising  
14 a combination of the detected expression levels of *laminin*  
15  $\alpha$ 4-specific mRNA and the at least one other mRNA species  
16 specific to the growth factor-related gene or to the  
17 structural gene other than a laminin gene; and  
18                   (d) comparing the expression profile in (c) to an expression  
19 profile for a normal tissue control, wherein a level of  
20 overexpression of *laminin*  $\alpha$ 4-specific mRNA, with respect  
21 to the control, is indicative of the presence of and ~~relatively~~  
22 ~~high degree of~~ invasiveness of the tumor in the subject,  
23 wherein a level of overexpression of the structural gene  
24 other than a laminin gene, with respect to the control, is  
25 indicative of ~~relatively high degree of~~ tumor invasiveness,  
26 and wherein a level of overexpression of the growth factor-  
27 related gene, with respect to the control, is indicative of

28                   ~~relatively high~~ degree of tumor aggressiveness.

29

1                   61. (Original Claim)   The method of Claim 60, wherein the  
2 growth factor-related gene encodes a protein selected from the group  
3 consisting of insulin-like growth factor binding protein precursor 3,  
4 transforming growth factor- $\beta$ -induced gene, vascular endothelial growth factor,  
5 connective tissue growth factor, human insulin-like growth factor binding  
6 protein precursor 5, placental growth factor, transcription factor Ap-2, human  
7 insulin-like growth factor II, and epidermal growth factor receptor.

1                   62. (Original Claim)   The method of Claim 60, wherein the  
2 structural gene encodes a protein selected from the group consisting of matrix  
3 metalloproteinase-2, keratin 18, vimentin, fibronectin 1, phospholipase A2  
4 receptor, desmoplakin, tropomodulin, tenascin C, and collagen type IV  $\alpha$ 1  
5 chain.

1                   63. (Original Claim)   The method of Claim 60, wherein the  
2 expression level of *laminin*  $\alpha$ 4-specific mRNA is detected by measuring RNA.

1                   64. (Original Claim)   The method of Claim 60, wherein the  
2 expression level of *laminin*  $\alpha$ 4-specific mRNA is detected by measuring cDNA.

1                   65. (Original Claim)   The method of Claim 60, wherein a  
2 gene expression microarray is used to detect the level of expression of *laminin*  
3  $\alpha$ 4-specific mRNA.

1                    66. (Original Claim)    The method of Claim 60, further  
2   comprising detecting the overexpression of *laminin*  $\beta 1$ -specific mRNA relative  
3   to the normal tissue control.

1                    67. (Original Claim)    The method of Claim 60, wherein the  
2   tissue sample is brain tissue.

1                    68. (Original Claim)    The method of Claim 60, wherein the  
2   tumor is a glial tumor.

Claims 69-74 have been cancelled.

1                    75. (Previously Added) The new method of Claim 1, further  
2   comprising detecting the overexpression of a gene encoding laminin  $\beta 1$  subunit  
3   relative to the normal control.

1                    76. (Previously Added) The method of Claim 18, further  
2   comprising detecting the overexpression of a gene encoding laminin  $\beta 1$  subunit  
3   relative to the normal control.

1                    77. (Previously Added) The method of Claim 28, further  
2   comprising detecting the overexpression of a gene encoding laminin  $\beta 1$  subunit  
3   relative to the normal control.

1                    78. (Previously Added) The method of Claim 44, further  
2 comprising detecting the overexpression of a gene encoding laminin  $\beta$ 1 subunit  
3 relative to the normal control.